

Priority

The Examiner has stated that the current application lacks the necessary reference to the prior application and suggested that Applicants amend the specification to include a statement reading "This is a continuation of Application No. 09/025151, filed 2/18/98" as the first sentence of the specification. Applicants respectfully request clarification, as no priority claim was made in the initial filing.

Specification

The Examiner has objected to the specification because of the listing of attorney docket numbers is improper. Applicants have deleted the attorney docket numbers in the specification.

35 U.S.C. § 112 Rejection

The Examiner has rejected claim 20 under 35 U.S.C. 112, second paragraph because it recites synthesizing and depends on claim 1 and 6. Applicants have amended claim 20 to clarify to "...after the synthesizing of primer extension products with a nucleic polymerase." Therefore, this rejection of claim 20 is obviated.

Anticipation Rejection Under 35 U.S.C. § 102(b)

The Examiner has rejected claims 1 & 2 under 35 U.S.C. 102(b) as being anticipated by Mitsunashi *et. al.* (US 5,580,971, Dec. 3, 1996). Applicants respectfully traverse this rejection.

In order to support anticipation under 35 U.S.C. §102(b), each and every element of a claimed invention must be disclosed within a single prior art reference.

In Mitsunashi *et. al.*, a biological sample is contacted with a first common polynucleotide primer in the solution whereas in the claimed invention, a biological sample is hybridized with a substrate, wherein the substrate has a plurality of different probes that are immobilized on a substrate. Consequently, Mitsunashi *et. al.* does not teach every element of the claimed invention. Therefore, this rejection under 102(b) should be withdrawn.

Obviousness Rejection Under 35 U.S.C. §103(a)

The Examiner has rejected claims 1-5 under 35 U.S.C. 103(a) as being unpatentable over Caskey *et. al.* (US 6,153,379 Nov. 28, 2000) in view of Chetverin *et. al.* (US 6,103,463 August 15, 2000). Applicants respectfully traverse the rejections.

Caskey *et. al.* teaches annealed primers are subjected to a single base extension reaction whereas in the claimed invention, annealed primers are subjected to multiple base extension reactions. Caskey *et. al.* would not work with multiple base extension reactions because the design of the method discussed by Caskey *et. al.* is for determining terminating nucleotides using dideoxynucleotides.

Chetverin *et. al.* teaches cellular RNAs are directly hybridized according to their poly (A)-tailed 3' termini to a sectioned binary array and is extended by incubation with a reverse transcriptase or DNA Polymerase using the hybridized RNA as a template. The extension products are sorted and amplified cDNAs of all cellular mRNAs. In contrast, our claims are directed to a process for detecting the presence of specific transcripts. Moreover, there is no suggestion or motivation, either in the references themselves (Chetverin *et. al.* and Caskey *et. al.*) or in the knowledge to one of ordinary skill in the art to combine reverse transcriptase to a method of detecting single base extension of a set of specific oligonucleotide primers.

Claims 6-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Caskey *et. al.* (US 6,153,379 Nov. 28, 2000) in view of Chetverin *et. al.* (US 6,103,463 August 15, 2000) in further view of Chee *et. al.* (US 5,861,242 Jan. 19, 1999). Applicants respectfully traverse the rejections.

Applicants earlier stated that Caskey *et. al.* discusses single base extension whereas the claimed invention teaches multiple base primer extension reactions. Caskey *et. al.* teaches away from the current invention and therefore, there is no motivation or suggestion, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to combine the Caskey *et. al.* with other references.

Claims 3-20, 26 & 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mitsuhashi *et. al.* (US 5,580,971 Dec. 3, 1996) in view of Chee *et. al.* (US 5,861,242 Jan. 19, 1999). Applicants assume that the Examiner intends to include Caskey *et. al.* as one of the references that can alleged be combined, because the

Examiner mentions the Caskey *et. al.* reference later. Applicants respectfully traverse the rejections.

In Mitsuhashi *et. al.*, Applicants had earlier stated that a biological sample is contacted with a first common polynucleotide primer in the solution whereas in the claimed invention, a biological sample is hybridized with a substrate, wherein the substrate has a plurality of different probes that are immobilized on a substrate. Therefore, the Mitsuhashi *et. al.* teaches away from the current invention and therefore, there is no motivation or suggestion, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to combine Mitsuhashi *et. al.* with Chee *et. al.*.

For the above reasons, applicants respectfully submit that the Examiner has failed to establish prima facie obviousness case of the rejected claims. The rejection under 35 U.S.C. § 103(a) should be withdrawn.

CONCLUSION

For these reasons, Applicants believe all pending claims are now in condition for allowance and should be passed to issue. If the Examiner feels that a telephone conference would in any way expedite the prosecution of the application, please do not hesitate to call the undersigned at (408) 731-5699.

The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account 01-0431.

If the Examiner has any questions pertaining to this application, the Examiner is requested to contact the undersigned attorney.

I hereby certify that this correspondence is being deposited by Express Mail to: Commissioner For Patents, Washington, D.C. 20231 On <u>June 13, 2002</u> Express Mail No.: <u>EU 373 655 356 US</u> AFFYMETRIX, INC. By: <u>[Signature]</u>
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Respectfully submitted,

[Signature]

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VERSION WITH MARKINGS TO SHOW CHANGES
MADE TO THE APPLICATION

In the Specification

On page 34, paragraph 3 of the specification, please delete [...attorney docket number 3357.1_____, attorney docket number 3298.1 _____, attorney docket number 3309_____, attorney docket number 3364, and _____, attorney docket number 3369.1..."]

In the Claims

Please amend Claim 1 as follows:

1. (amended) A method for detecting a plurality of RNAs in a sample comprising:
 - hybridizing the sample with a substrate, wherein the substrate has a plurality of different probes and wherein the probes are suitable for multiple bases primer extension reactions;
 - synthesizing primer extension primer products with a nucleic acid polymerase, appropriate reagents and conditions, from the primers and using the RNAs as templates; and
 - detecting the primer extension products.

20. (amended) The method of claim 18 wherein the label is attached to the extension products after the synthesizing of primer extension products with a nucleic acid polymerase.

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